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09/603,713	06/27/2000	Jordan J.N. Tang	2932.1008-000	4604

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EXAMINER
MOHAMED, ABDEL A

ART UNIT	PAPER NUMBER
1653	27

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/603,713	TANG ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *17* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *25* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

ACKNOWLEDGMENT OF AMENDMENTS, REMARKS, IDS AND STATUS OF THE CLAIMS

1. The amendment and remarks filed 12/24/02 and the supplemental amendment and remarks filed 3/24/03, respectively, and the Information Disclosure Statement with Form PTO-1449 filed 7/23/02 (Paper No. 17) are acknowledged, entered and considered. In view of Applicant's request claims 1-27 have been canceled and claims 28-40 have been added. Thus, claims 28-40 are now pending in the application. With respect to the IDS and Form PTO-1449 filed 9/27/02 (Paper No. 18) and 2/11/03 (Paper No. 24), respectively, they are not considered and signed as requested by Applicant because the references cited therewith are not with the application. The references cited on the IDS filed 9/27/02 and 2/11/03 (Paper Nos. 18 and 24, respectively) should be provided. The objection to the trademark and the rejections to 35 U.S.C. 112, second paragraph and 35 U.S.C. 102(b) over the prior art of record for claims 1-2, 10 and 16-17 have been withdrawn in view of Applicant's amendment, remarks and cancellation of the claims filed 12/24/02 and 3/24/03, respectively. However, the rejection under 35 U.S.C. 112, first paragraph for newly submitted claims 28-40 is maintained. It is noted that the reaction under 35 U.S.C. 112, first paragraph for canceled claims 1-3, 5, 10-17 and 20-23 is withdrawn in favor to the rejection under 35 U.S.C. 112, first paragraph for the newly presented claims 28-40. This is not a new rejection since Applicant has received the 112, first paragraph rejection in the previous Office action mailed 6/17/02 as Paper No. 16. Further, Applicant has amended the

claims and because of the amendment, a new ground of rejection is necessitated. Thus, this does not preclude the Examiner from making this Office action Final and the Examiner will respond to Applicant's arguments as they apply to the rejection set forth.

CLAIMS REJECTION-35 U.S.C. 112 [1st] PARAGRAPH.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly presented claims 28-40 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound having a structure of OM99-2 and a pharmaceutically acceptable salts thereof and inhibition of memapsin 2 by OM99-1 and OM99-2 inhibitors and use of said inhibitors in designing, synthesizing and/or preparing the Leu*Ala dipeptide isostere and testing of inhibitory activity toward the enzyme *in vitro*, does not reasonably provide enablement for a product defined by reference to a desirable characteristic or property, namely structures disclosed in claim 37 e) and claim 40 a) and to a method for treating a patient to decrease the likelihood of developing or progressing of Alzheimer's disease by administering to the individual an effective amount of memapsin 2 in the manner claimed in claims 34-36. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not adequately teach an inhibitor of catalytically active memapsin 2 product defined by reference to a desirable characteristic or property by fitting into the catalytical cleft of memapsin 2 useful for treatment and/or prevention of Alzheimer's disease as presently claimed in claims 28-40; rather, the specification teaches the use of memapsin 2 in a method of cloning (Example 1), distribution (Example 2), expression, refolding and purification (Example 3), proteolytic activity (Example 4), activation (Example 5), Expression in mammalian cells (Example 6), design and synthesis (Example 7), and measurement of enzymatic activity *in vitro* (Example 8).

Therefore, the instant specification does not commensurate with the claimed subject matter in which the compounds used as potent inhibitors of catalytically active memapsin 2 are expected to be particularly useful in the treatment and/or prevention of Alzheimer's disease. Thus, there is no evidence or data to show that a similar regimen can be used for treating a patient to decrease the likelihood of developing or the progression of Alzheimer's disease by administering to the individual an effective amount of an inhibitor of memapsin 2 having an K_i of less than or equal to 10^{-7} M or which binds to crystallized enzyme characterized by the parameters in Table 2 when bound to OM99-2. Also, a method for preparing a Leu* Ala dipeptide isostere wherein the chemical structures included therewith in the compounds have been disclosed in the instant specification and claimed in claims 37 to 40, however, the structures of claim 37 e) and claim 40 a) could not be searched as products and/or as reactants in commercial data base (e.g., CAS registry). Further, the above structures (i.e., the structures

claimed in claim 37 e) and 40 a)) are not disclosed in the instant specification in the manner claimed.

Thus, in view of the above, and in view of the fact that there is no enablement in the instant specification for the method of treating an/or preventing of Alzheimer's disease by administering the effective amount of a compound of claim 28, and further in view of the complexity of Applicant's invention and the state of the art of treating and/or preventing of Alzheimer's disease, with the various compounds claimed; the Examiner is unable to determine the enablement of the invention as claimed without appropriate evidence or data. Such evidence in the art of treating cognitive dysfunctions details the state of the art in this area and establishes that even the disease is very hard to diagnose. For example, Ezzell (Scientific America, pages 152-153, March 7, 1993) states on page 152, middle column, before last paragraph that doctors can only diagnose Alzheimer's through a process of elimination, ruling out other disorders such as a slight stroke, a brain tumor, or even an adverse drug reaction. A definitive diagnosis must await death and autopsy, when a pathologist can view the telltale "senile plaques" that pock the brains of Alzheimer's victim. Further, Varon et al. (Dev. Neurosci., Vol. 6, pp. 73-100, 1983/1984) discuss the implications of neurotrophic and neurite-promoting factor and their clinical potential in neuronal diseases such as Parkinson, ALS and Alzheimer in which the authors concluded by stating that further clinical progress requires a better understanding of neurobiological bases of nerve regeneration. Furthermore, Cordell et al. (U.S. Patent No. 5,221,607) discuss that the etiology of Alzheimer's disease is unknown and up to date, there are

no means available to treat the pathogenesis of Alzheimer's disease and the paucity of understanding concerning the mechanism of amyloid formation in Alzheimer's disease is a major obstacle in the development and design of therapeutic agents that can intervene in this process (See e.g., Col.1, lines 55-67). Similarly, Nelson et al. (U.S. Patent No. 5,252,463) discuss serious diseases affecting the central nervous system which referred as neuropathologies such as Alzheimer's disease and Down's Syndrome in which the etiology of Alzheimer's disease is unknown (See e.g., column 1). Thus, the prior art clearly show the unpredictable nature and the complexity of the art in regard to treatment and/or prevention of Alzheimer's disease. Therefore, considering the nature of the treatment and/or prevention of Alzheimer's disease by administering the inhibitors of memapsin 2 claimed and the limited success achieved; one skilled in the art would not accept the instantly claimed invention as obviously valid and correct without demonstration of evidence or data for the following reasons:

In view of the fact that animals and humans are outbred, in view of the lack of disclosure of suitable animal models for a method of diagnosing or treating or preventing cell death in the central or peripheral nervous system, in view of the recognized problems in the art regarding effective treatment of diseases affecting the nervous systems (neuropathologies) and in view of the fact that it is difficult to regenerate the neurons in the living body; a reasonable doubt exists as to the enablement of the claimed method of treating and/or preventing Alzheimer's disease in a subject and particularly in a human by administering the inhibitors of memapsin 2 claimed. Thus, the claims are based on pure speculation that the method would be effective since

Applicant has not established any *nexus* between the various claimed inhibitors of memapsin 2 and their use in the manner claimed.

Further, the first paragraph of 35 U.S.C. 112 requires, inter alia, that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not directed to disclose every species that falls within a generic claim, id. At 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, in view of the above, and in view of the fact that there is no enablement in the instant specification for treating and/or preventing Alzheimer's disease by administering inhibitors of memapsin 2. Thus, applying the Wands factors to the facts of this case, one of skill in the art would find that undue amount of experimentation would be required to practice the full

scope of the extremely broad claims fro the reasons given above. Hence, in view of the quantity of experimentation necessary, the lack of adequate guidance or working examples or data, and the breadth of the claims, the claims are not commensurate in scope with the enabling disclosure. Accordingly, filing of evidence commensurate with the scope of the claims or amendment of the claims to what is supported by the enabling disclosure is suggested.

ARGUMENTS ARE NOT PERSUASIVE

CLAIMS REJECTION-35 U.S.C. 112 [1st] PARAGRAPH.

3. The rejection of newly submitted claims 28-40 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound having a structure of OM99-2 and a pharmaceutically acceptable salts thereof and inhibition of memapsin 2 by OM99-1 and OM99-2 inhibitors and use of said inhibitors in designing, synthesizing and/or preparing the Leu*Ala dipeptide isostere and testing of inhibitory activity toward the enzyme *in vitro*, does not reasonably provide enablement for a product defined by reference to a desirable characteristic or property, namely structures disclosed in claim 37 e) and claim 40 a) and to a method for treating a patient to decrease the likelihood of developing or progressing of Alzheimer's disease by administering to the individual an effective amount of memapsin 2 in the manner claimed in claims 34-36. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments and Exhibits A and B attached herewith to confirm the predictability of the animal models and further to demonstrate the efficacy of the claimed compounds in enhancing memory storage and long-term potentiation have been considered but they are not persuasive. Applicant has argued that 1) the Examiner has not made a *prima facie* case for lack of enablement; 2) even if one assumes it is made, the rejection is effectively rebutted by Applicant's remarks and the enclosed attached publication; 3) the legal standard imposed by 35 U.S.C. § 112, first paragraph has been met because Applicant through detailed objective guidance and examples as disclosed in the present specification teaches the manner and process of making and using the invention in terms commensurate in scope with the claims; 4) that compounds of the invention inhibit the activity of memapsin 2 and thereby inhibit formation of amyloid β-protein, and as such improve cognitive function such as memory and learning ability in a patient, hence, Applicant's claimed method is applicable to cognitive dysfunctions such as Alzheimer's disease because it improves long-term potentiation in hippocampal cells and, thus, causes increased memory retention and learning ability; 5) Applicant's animal models provide guidance as to the dosage, the time frame for administering the compound, and thus, Applicant's animal model for memory retention is applicable to humans as well as other patients, and as such, there is insufficient evidence to support the rejection as set forth in the Official Action, that one having ordinary skill in the art could practice the claimed invention without undue experimentation; and 6) concludes by stating that the specification provides a full evidence consistent with description in the specification which enables the full scope of the present

invention, and as such, the claims are fully enabled by the specification as originally filed, and that the requirements of the first paragraph of 35 U.S.C. § 112 have been met is not persuasive.

With respect to the predictability or unpredictable nature of the claimed compound, Applicant has argued on pages 13-14 of the remarks filed on 12/24/02 (Paper No. 23) that compounds that are permeable to the blood-brain barrier will be able to penetrate tissue in the body where memapsin 2 is found, and such compounds will block cleavage of APP by memapsin 2 under physiological conditions. Thus, since memapsin 2 has been shown to be responsible for the production of amyloid β-protein and increased activity of memapsin 2 has been shown to increase the accumulation of amyloid β-protein and cause early onset of Alzheimer's disease, decreasing the activity of memapsin 2 will reduce the accumulation of amyloid β-protein thereby reducing the likelihood of developing Alzheimer's disease or halting further progression of the disease in patients who already have the disease. As such, Applicants have established a *nexus* between compounds that include the structural formula of OM99-2 and the treatment or prevention of Alzheimer's disease by showing that these compounds inhibit the activity of memapsin 2, and thus, inhibit the production of amyloid β-protein is not persuasive.

Contrary to Applicant's arguments as discussed above that there is no evidence or data to show that a similar regimen can be used for treating a patient to decrease the likelihood of developing or the progression of Alzheimer's disease by administering to the individual an effective amount of an inhibitor of memapsin 2 having an K_i of less than or equal to 10^{-7} M or which binds to crystallized enzyme characterized by the parameters in Table 2 when bound to

OM99-2. Also, a method for preparing a Leu* Ala dipeptide isostere and the chemical structures included therewith in the compounds have been disclosed in the instant specification and claimed in claims 37 to 40, however, the structures of claim 37 e) and claim 40 a) could not be searched as products and as reactants in commercial data base (e.g., CAS registry). Further, the above structures (i.e., the structures claimed in claim 37 e) and 40 a)) are not disclosed in the instant specification as claimed. Thus, the scope of the instantly claimed invention are very broad and speculative in that there is/are no working example(s) or data or evidence which shows that the claimed pharmaceutical formulation comprising the compounds claimed in a method for treating a patient to decrease the likelihood of developing or the progression of Alzheimer's disease by administering therapeutically effective amount of said formulation thereof.

The scope of the claims include pharmaceutical formulations comprising all kinds of variations as recited in claims 29-33; and to methods of treating and/or preventing the development or progression of Alzheimer's disease by administering the above pharmaceutical formulations thereof as claimed in claims 34-36. The specification nor the attached publications intended to support the claimed invention disclose one reasonable method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claims. The specification including the publications provided to support the enablement issue lacks guidance/direction as to how to employ a pharmaceutical preparation useful for treatment of a patient to decrease the likelihood of developing or the progression of Alzheimer's disease by administering to said patient an effective amount of a compound according to claim 28 in the

manner claimed in claims 34-36. Thus, there is no evidence in the instant specification to use or administer the pharmaceutical formulation in therapeutically effective composition as claimed.

The publications provided (Exhibit A: Science News, Vol. 141, pp 152-153, 1993, particularly page 153, Col. 3, paragraph 2 and 3) have been considered and appears to support that amyloid β-protein is a major constituent of the plaques found in high concentrations in the brains of Alzheimer's patients; however, the amyloid β-protein ***has <u>not</u> been shown*** to be toxic to nerve cells because it increases the calcium influx as argued by Applicant on page 13, last paragraph on the remarks filed 12/24/02 (Paper No. 23). Rather, the publication states clearly that β-amyloid itself produced ***<u>no</u>*** toxic effects, although, it increased the calcium influx mediated by glutamate (See e.g., page 153, Col. 3, paragraph 3). The publication further states on page 152, Col. 3, paragraph 1, that researchers have so far not determined the function of amyloid precursor protein (APP) which is embedded in the outer cell membrane and concludes on page 153, Col. 3, last paragraph by stating that Alzheimer's researchers will continue to focus their inquiries on beta amyloid for some time to come....."And we are going to keep on going until we figure out how to stop it". Thus, clearly showing the unpredictable nature of the compounds in the method of treatment claimed. For support to show the complexity of Applicant's invention and the state of the art of treating and/or preventing Alzheimer's disease, see the prior art cited in the previous Office action. For further support, WO 01/70672 (Published 9/27/01) states on page 3, lines 8-11, that there is an urgent need for pharmaceutical agents capable of slowing the progression of Alzheimer's disease and/or preventing it in the first

place; however, at present there are no effective treatments for halting, preventing, or reversing the progression of Alzheimer's disease. Furthermore, Hook (U.S. Patent No. 6,245,884) states on column 1, lines 49-55 that no methods of preventing Alzheimer's disease or Alzheimer's-type dementia (AD) is known and treatment is primarily is supportive, such as that provided by a family member in attendance. Simulated memory exercises on a regular basis have been shown to slow, but not stop, memory loss. A few drugs, such as tacrine, result in a modest temporary improvement of cognition but do not stop the progression of dementia. Therefore, the cited prior art clearly show the unpredictable nature and the complexity of the art in regard to treatment of cognitive dysfunctions which includes Alzheimer's disease.

Thus, in view of the above and in view of the fact that there is no working example or data or evidence which shows that the claimed compounds are useful as pharmaceutical formulations in the method of treatments as claimed in claims 34-36. Although, there is preparation Examples for pharmaceutical formulations as well as *in vitro* assays and certain mode of administration. Nevertheless, there is no evidence in the instant specification nor in the publications provided to use or administer the pharmaceutical formulations in therapeutically effective amount as claimed, except for the mere recitation of protocols on pages 24-27 in the instant specification contemplating the suitable dosage of the compound to be administered generally in patients which includes human for the intended treatment and/or prevention or slowing progression of Alzheimer's disease. Further, there are no sufficient data or evidence to substantiate such protocols of using pharmaceutical formulations of claim 28 in the manner

claimed in claims 34-36. Hence, the only support for the claimed pharmaceutical formulations in the specification and method of treatment thereof is Applicant's supposition of the invention as recited in the protocols. Thus, in view of the above, it would include those that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since **all kinds** of pharmaceutical formulations comprising the various compounds in a method for treatment of a patient to decrease the likelihood of developing or the progression of Alzheimer's disease are contemplated and are encompassed as well as wide range of situations. The results desired appear to be highly dependent on all variables, the relationship of which are not clearly disclosed. Hence, one of ordinary skill in the art would not be able reproduce all the aspects the claimed invention pharmaceutical formulations as well as methods for treatment and/or prevention of Alzheimer's disease as encompassed in the claims would be effective and under what conditions.

Therefore, in view of the above, the scope of the pharmaceutical formulation with various compounds are useful in a method for treating a patient to decrease the likelihood of developing or progression of Alzheimer's disease by administering to the individual an effective amount of memapsin 2 intended to be effective for the claimed purpose as encompassed in the claims would be effective and under what conditions. The Examiner is unable to determine the enablement of the invention as claimed without appropriate working examples. The only support for the claimed invention in the specification is Applicant's supposition of the invention and the

improper incorporation of several publications attached herewith supporting the protocols disclosed in the instant specification. Secondly, the Examiner has clearly shown in the previous Office Action of Paper No. 16 (mailed 6/17/02) and as discussed above that without guidance through working example(s), one of ordinary skill in the art would not predict from background discussion and/or information and protocols to employ or administer the pharmaceutical formulation in therapeutically effective composition in the manner claimed. Thus, the specification does not enable any person skilled in the art to which it pertains, or which it is most nearly connected, to use the invention commensurate in scope with the claims. In the express absence of one or more examples, evidence and sufficient guidance, the skilled artisan would be faced with undue experimentation for practicing the invention. Thirdly, it is not understood from Applicant's response how the instant invention, which Applicant considers as novel and inventive, be exemplified without working example(s) or data or evidence. The law requires that a disclosure in an application shall inform those skilled in the art how to use Applicant's alleged discovery, not how to find out how to use it for themselves. See *In re Gardner et al.*, 166 USPQ 138 (CCPA 1970). Therefore, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled. Hence, it is viewed that the specification does not enable the invention as claimed in claims 28-40, as it does not teach how to use the invention to achieve the function of the claims for the reasons discussed above. Thus, applying the Wands factors to the facts of this case, one of skill in the art would find that undue amount of experimentation would be required to practice the full scope of the extremely

broad claims fro the reasons given above. Hence, in view of the quantity of experimentation necessary, the lack of adequate guidance or working examples or data, and the breadth of the claims, the claims are not commensurate in scope with the enabling disclosure. Accordingly, filing of evidence commensurate with the scope of the claims or amendment of the claims to what is supported by the enabling disclosure is again suggested.

The following is a new ground of rejection necessitated by Applicant's amendment"

CLAIMS REJECTION-35 U.S.C. 112 [2nd] PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 35 and 36 recite the limitation "the inhibitor" in line 1, respectively. There is insufficient antecedent basis for this limitation in claim 36 or claim 35 or claim 34 or claim 28.

ACTION IS FINAL, NECESSITATED BY AMENDMENT

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CONCLUSION WITH FUTURE CORRESPONDENCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The appropriate fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher S. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Mohamed/AAM

June 25, 2003